REMARKS/ARGUMENTS

Claims 1-10 are pending. Claims 1-10 have been rejected. Claim 1 has been amended. Support for the amendments may at least be found at page 6, lines 7-12, and page 42, line 10 through page 43, line 13 in the specification as filed. No new matter has been entered as a result of the entry of these amendments.

Rejection under 35 U.S.C. §112, second paragraph

The Examiner rejected claims 1-10 under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicants' claims 2-10 all ultimately depend upon amended independent claim 1.

The Examiner expressed the belief that it is not clear what Applicant means by the claim term "protective" and what is encompassed by the claim term "protective".

Applicants have amended independent claim 1. The liver protection effect of the sample can be determined more precisely by measuring apoptosis inhibition effect of hepatocyte using the activity inhibiting hepatocyte DNA cleavage as an index, and by measuring the 24 hour survival rate of the mouse as disclosed at page 6, lines 7-12 of Applicants' specification. Also, as demonstrated in

Example 6, the water extract obtained from the root or stem of *Acanthopanax koreanum* has an efficacy to inhibit apoptosis of the liver cell as disclosed at page 43, lines 10-13 of Applicants' specification.

In light of the foregoing amendments, Applicants respectfully request the Examiner withdraw the rejection of claims 1-10 under 35 U.S.C. §112, second paragraph, and find that claims 1-10 are allowable.

Rejections under 35 U.S.C. §§102(b)/103(a)

The Examiner asserts claims 1-10 are rejected under 35 U.S.C. §102(b) as anticipated by or, in the alternative, under 35 U.S.C. §103(a) as obvious over U.S.P.N. 6,365,768 to Palladino (hereinafter Paladino).

In framing this rejection, the Examiner stated the following:

> "Applicant's claims are drawn to product-by-process claims. The product is an extract from *Acanthopanax koreanum* stem or root. Regarding product-by-process claims, note that MPEP § 2113 states that:
>
> > 'the prior art discloses a product which reasonably appears to be either identical with or only slightly different than a product claimed in a product-by-process claim, a rejection based alternatively on either section 35 U.S.C. 102 or 35 U.S.C. 103 of the statute is appropriate.. .A lesser burden of proof is required to make out a case of prima facie obviousness for product-by-process claims because of their peculiar nature than when a product is claimed in the conventional fashion. In re Brown, 59 CCPA 1063, 173 USPQ 685 (1972); In re Fessmann, 180 USPQ 324 (CCPA1 974)... Once the Examiner provides a rationale tending

> to show that the claimed product appears to be the same or similar to that of the prior art, although produced by a different process, the burden shifts to Applicant to come forward with evidence establishing an unobvious difference between the claimed product and the prior art product. In re Marosi, 710 F.2d 798, 802, 218 USPQ 289, 292 (Fed. Cir. 1983)."
> Palladino et al. (6,365,768) teach using an extract of *Acanthopanax koreanum* to inhibit Tumor Necrosis Factor-a (i.e. TNF-a), which can be attributed to viral infections such as hepatitis viruses and cirrhosis (column 2, lines 4-5; column 14, lines 29-33; column 22, lines 19-37).'
> The reference does not specifically teach that the product is extracted using the method claimed by Applicant in claim 1 or that the extract contains all of the characteristics claimed in claims 2, 3 and 4. However, the reference product reasonably appears to be the same product as claimed because the reference product is extracted from the same source as claimed and has the same TNF-a (i.e. Tumor Necrosis Factor-a inhibitory activity and viral infection (i.e. hepatitis)) is claimed.
> However, even if the reference extract and the claimed extract are not one and the same and there is, in fact, no anticipation, the reference extract would, nevertheless, have rendered the claimed extract obvious to one of ordinary skill in the art at the time the claimed invention was made in view of the clearly close relationship between the extract as evidence by their shared TNF-a (i.e. Tumor Necrosis Factor- a inhibitory activity and viral infection (i.e. hepatitis))."

Palladino teaches acanthoic acid is a suspected effector of both Interleukin-a and TNF-α. Palladino teaches further at col. 20, lines 61-66 that acanthoic acid is extracted and isolated, at least in the form of a crude extract comprising acanthoic acid, from the root bark of *Acanthopanax koreanum* Nakai. According to Palladino at col. 20, line 60 through col. 21, line 61, dried root bark of *Acanthopanax koreanum* Nakai may be produced according to the following method:

dried root bark of *Acanthopanax koreanum* Nakai is obtained, chipped and covered with between 1L to 3L, and preferably 2L, of a suitable solvent, most preferably methanol.

The inventor, Jung Joon Lee, has conducted experiments to establish that a water extract taken from either the root or stem of Acanthopanax Koreanum as recited in claims 1-10 does not contain acanthoic acid. For purposes of comparison, the inventor also conducted experiments to establish that an ethanol extract taken from either the root or stem of *Acanthopanax Koreanum* does contain acanthoic acid.

The inventor, Jung Joon Lee, submits a declaration under 37 C.F.R. §1.132 reciting the experimental procedures, results obtained, and a comparison made between the claimed subject matter of claims 1-10 and the prior art of record.

The preparation of a water extract from the root of *Acanthopanax Koreanum* (Sample 1) was conducted as follows: A root of *Acanthopanax Koreanum* was dried and sliced into small pieces. A 10-L round-bottomed flask was charged with 1 kg of sliced root and a quantity of water. The sliced root and water were mixed and extracted at a temperature of greater than 90°C for 3 hours. The extraction was repeated two times. The extracted solution was filtered through filtrate membranes, concentrated under a reduced pressure in a rotary evaporator, and lyophilized to yield a water extract from the root of

Acanthopanax Koreanum weighing 142 g.

The preparation of an ethanol extract from the root of the *Acanthopanax Koreanum* (Sample 2) was conducted as follows: The root of *Acanthopanax Koreanum* was dried and sliced into small pieces. A 2-L round-bottomed flask fitted with a reflux condenser was charged with 0.1 kg of sliced root and 500 mL of ethanol. The sliced root and ethanol were mixed, heated at a temperature of 80°C for 5 hours using a heating mantle, and extracted. The extracted solution was filtered through filtrate membranes, concentrated using a rotary evaporator, and dried under a reduced pressure in a vacuum oven to yield an ethanol extract from the root of *Acanthopanax Koreanum* weighing 5 g.

The preparation of a water extract from the stem of the *Acanthopanax Koreanum* (Sample 3) was conducted as follows: The stem of *Acanthopanax Koreanum* was dried and sliced into small pieces. A 10-L round-bottomed flask was charged with 1 kg of sliced root and a quantity of water. The sliced root and water were mixed and extracted at a temperature of greater than 90°C for 3 hours. The extraction was repeated two times. The extracted solution was filtered through filtrate membranes and concentrated under reduced pressure in a rotary evaporator, and lyophilized to yield a water extract from the stem of *Acanthopanax Koreanum* weighing 80 g.

The preparation of an ethanol extract from the stem of *Acanthopanax Koreanum* (Sample 4) was conducted as follows: The stem

of *Acanthopanax Koreanum* was dried and sliced into small pieces. A 2-L round-bottomed flask fitted with a reflex condenser was charged with 0.1 kg of sliced root and a 500 mL of ethanol. The sliced root and ethanol were mixed, heated at a temperature of 80°C for 5 hours using a heating mantle, and extracted. The extracted solution was filtered through filtrate membranes, concentrated using a rotary evaporator, and dried under reduced pressure in a vacuum oven to yield an ethanol extract from the stem of *Acanthopanax Koreanum* weighing 3 g.

Each sample 1-4 was prepared for HPLC analysis using an HPLC commercially available from the Dionex Corporation of Sunnyvale, Canada. The HPLC was composed of a Dionex PDA Photodiode Array Detector, an ASI-100 Automated Sample Injector, a P580 pump, a J'sphere ODS-H80 Column (250mm x 4.6mm I.D.). The HPLC tests were conducted using sample injections measuring 20 μl, a solvent mixture of acetonitrile (ACN) and water 10% (volume/volume, ACN to water) to 100% (volume/volume, ACN to water) gradient, 60 min. The flow rate was 1 ml/min., and the detection wavelength was 207 nm.

The HPLC test of sample 1 was conducted as follows: A portion of sample 1 was solubilized in pure methanol, for final concentration of analyzed sample 1 to be 1 mg/ml. An HPLC chromatogram of sample 1 is shown in Exhibit A attached hereto. The HPLC test of sample 2 was conducted as follows: A portion of sample 2 was solubilized in pure

methanol, for final concentration of analyzed sample 2 to be 1 mg/ml. An HPLC chromatogram of sample 2 is shown in Exhibit A attached hereto. The HPLC test of sample 3 was conducted as follows: A portion of sample 3 was solubilized in pure methanol, for final concentration of analyzed sample 3 to be 1 mg/ml. An HPLC chromatogram of sample 3 is shown in Exhibit B attached hereto. The HPLC test of sample 4 was conducted as follows: A portion of sample 4 was solubilized in pure methanol, for final concentration of analyzed sample 4 to be 1 mg/ml. An HPLC chromatogram of sample 4 is shown in Exhibit B attached hereto.

The inventor, Jung Joon Lee, also prepared six standard solutions of several compounds (of Exhibit C attached hereto) identified as "EE" (Table 1), "EB" (Table 2), "TA" (Table 3), "Sy" (Table 4), "AA" (Table 5), and "KA" (Table 6) for quantitative analysis. Each standard solution was prepared for final concentration shown in Tables 1-6, respectively. Each standard solution underwent HPLC testing. The HPLC analysis of each standard solution was accomplished and the concentration-area was plotted as a standard curve of Tables 1-6 attached hereto. The standard curve was used to measure the quantity of the content of each standard solution. The HPLC results of the water extracts from both the root and stem of *Acanthopanax Koreanum* shown in Exhibits A and B demonstrate the absence of acanthoic acid. The HPLC results of the ethanol extracts

from both the root and stem of *Acanthopanax Koreanum* shown in Exhibits A and B demonstrate the presence of acanthoic acid.

The disclosure of U.S. Patent No. 6,365,768 to Palladino et al. teaches extracting and isolating acanthoic acid, at least in the form of a crude extract containing acanthoic acid, from the root bark of *Acanthopanax koreanum* Nakai. The disclosure of U.S. Patent No. 6,365,768 to Palladino et al. teaches the extract of paragraph 17 may produced according to the following method: dried root bark of *Acanthopanax koreanum* Nakai chipped and covered with 1L to 3L of a suitable solvent, most preferably methanol (col. 20, l. 66-col. 21, l. 10). The methanol extract from the root bark of *Acanthopanax koreanum* Nakai taught by Palladino contains acanthoic acid, while the experiments set forth herein that the inventor, Jung Joon Lee, conducted demonstrate that water extracts from the both the root and stem of *Acanthopanax koreanum* shown in Exhibits A and B do not contain acanthoic acid.

The results of these experiments demonstrate conclusively that the Palladino reference does not anticipate claims 1-10 of the present application and an unobvious difference exists between the subject matter of Applicants' claims 1-10 and Palladino.

In addition, Palladino teaches that acanthoic acid is a suspected effector of both Interleukin-a and TNF-α. In particular, Palladino teaches acanthoic acid is obtained from the alcohol extract

from the root of *Acanthopanax koreanum*.

Applicants draw the Examiner's attention to experimental example 3 disclosed in Applicants' specification. The serum level of TNF-α is measured in liver-injury mice model induced by D-GalN/LPS (page 32, line 25 through page 36, line 12). Tables 4 and 5 demonstrate that the water extract of Applicants' claims 1-10, that is, the water extract from the root or stem of *Acanthopanax koreanum*, exhibits excellent effect on TNF-α, compared with ethanol extract (70% ethanol extract). According to Palladino, the ethanol extract contains acanthoic acid, the content being taught in the reference. Applicants would also draw the Examiner's attention to Tables 2 and 3 and page 32, lines 8-23 of Applicants' specification. The disclosure indicates that the 70% ethanol extract demonstrates no efficiency for the treatment of hepatitis, but in contrast the water extract of the claims 1-10 demonstrates excellent efficiency for treating hepatitis.

In light of the foregoing, Applicants respectfully request the Examiner withdraw the rejections under 35 U.S.C. §102(b)/§103(a) and find that claims 1-10 are allowable.

The Examiner rejected claims 1-10 under 35 U.S.C. §102(b) as anticipated by or, in the alternative, under 35 U.S.C. §103(a) as obvious over U.S.P.N. 5,900,434 to Pyun et al.

The inventor, Jung Joon Lee, has conducted experiments to establish that a water extract taken from either the root or stem of *Acanthopanax Koreanum* as recited in claims 1-10 does not contain acanthoic acid. For purposes of comparison, the inventor also conducted experiments to establish that an ethanol extract taken from either the root or stem of *Acanthopanax Koreanum* does contain acanthoic acid. The discussion concerning these experiments have been set forth above and the declaration under 37 C.F.R. §1.132 of Jung Joon Lee is submitted herewith.

The disclosure of U.S. Patent No. 5,900,434 to Pyun et al. teaches extracting and isolating acanthoic acid from the dried root bark of *Acanthopanax koreanum* Nakai. The disclosure of U.S. Patent No. 5,900,434 to Pyun et al. teaches the extract of paragraph 20 may be produced adding 1 kg of dried root bark to 1L to 3L of methanol (or diethyl ether or mixture thereof) (col. 3, l. 49-col. 4, l. 3). The methanol extract from the root bark of *Acanthopanax koreanum* Nakai taught by Pyun contains acanthoic acid, while the experiments set forth herein that the inventor, Jung Joon Lee, conducted demonstrate that water extracts from the both the root and stem of *Acanthopanax koreanum* shown in

Exhibits A and B do not contain acanthoic acid. These experiments demonstrate the methanol extracts taught by Pyun do not contain all of the characteristics claimed in claims 1-10 of the present application.

Applicants draw the Examiner's attention to experimental example 3 disclosed in Applicants' specification. The serum level of TNF-α is measured in liver-injury mice model induced by D-GalN/LPS (page 32, line 25 through page 36, line 12). Tables 4 and 5 demonstrate that the water extract of Applicants' claims 1-10, that is, the water extract from the root or stem of *Acanthopanax koreanum*, exhibits excellent effect on TNF-α, compared with ethanol extract (70% ethanol extract). According to Pyun, the ethanol extract contains acanthoic acid, the content being taught in the reference. Applicants would also draw the Examiner's attention to Tables 2 and 3 and page 32, lines 8-23 of Applicants' specification. The disclosure indicates that the 70% ethanol extract demonstrates no efficiency for the treatment of hepatitis, but in contrast the water extract of the claims 1-10 demonstrates excellent efficiency for treating hepatitis.

In light of the foregoing, Applicants respectfully request the Examiner withdraw the rejections under 35 U.S.C. §§102(b)/103(a) and find that claims 1-10 are allowable.

CONCLUSION

An earnest and thorough attempt has been made by the undersigned to resolve the outstanding issues in this case and place same in condition for allowance. If the Examiner has any questions or feels that a telephone or personal interview would be helpful in resolving any outstanding issues which remain in this application after consideration of this amendment, the Examiner is courteously invited to telephone the undersigned and the same would be gratefully appreciated.

It is submitted that the claims herein patentably define over the art relied on by the Examiner and early allowance of same is courteously solicited.

If any additional fees are required in connection with this case, it is respectfully requested that they be charged to Deposit Account No. 02-0184.

Respectfully submitted,

JUNG JOON LEE ET AL.

By _____

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Date: January 15, 2007

I, Antoinette Sullo, hereby certify that this correspondence is being deposited with the United States Postal Service as Express Mail in an envelope addressed to: "Mail Stop Amendments, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313" on January 15, 2007

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Antoinette Sullo